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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/742,346	12/19/2003	Robert Falotico	CRD-5062 USANP	6421
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PHILIP S. JOHNSON JOHNSON & JOHNSON ONE JOHNSON & JOHNSON PLAZA NEW BRUNSWICK, NJ 08933-7003			EXAMINER HELM, CARALYNNE E	
			ART UNIT 1609	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/742,346

Applicant(s)

FALOTICO ET AL.

Examiner

Caralynne Helm

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 12-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 3 sheets
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Note to Applicant: References to paragraphs in non-patent literature refers to full paragraphs (e.g. 'page 1 column 1 paragraph 1' refers to the first full paragraph on page 1 in column 1 of the reference)

Election/Restrictions

Applicant's election of the invention of Group I, claims 1-11, and the species trichostatin A, a polymeric coating and rapamycin, submitted April 23, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The requirement is deemed proper and is therefore made FINAL.

Claims 12-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Information Disclosure Statement

The European Search Report listed cannot be properly cited on form 1449 as it is not published and the date thereon is therefore not a date of publication. Thus, it was not considered as a reference of record.

Objections

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. Please note that the instant abstract currently exceeds the 150 word limit. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 4-7, and 9-11 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Tseng et al. (Pregrant Publication No. US 2005/0065596 A1) in light of Windecker et al. (Current Pharmaceutical Design) and Chudzik et al. (US Pregrant Publication No. US 2002/0188037 A1).

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In claim 1, Tseng et al. teach a stent (an implantable structure), containing drug depots capable of controllably delivering one or more histone deacetylase (HDAC) inhibitors (see claim 1). In addition, Tseng et al. also teach that the disclosed device delivering the HDAC inhibitors is particularly beneficial in the treatment of restenosis, implying that the HDAC inhibitors would be present at therapeutic dosages within the stent device (see paragraph 37). Tseng et al. go on to further describe the HDAC inhibitor included on or in the stent body as trichostatin A, abbreviated as TSA (see claims 12-14 and paragraph 15 lines 1-2). Also taught by Tseng et al. is the inclusion of an additional pharmaceutical agent or agents, such as anti-inflammatory and anti-proliferative agents, where an exemplary agent includes rapamycin (see paragraph 134 lines 1-4 and 12-13; claims 2 and 3). Tseng et al. does not specifically teach rapamycin as the preferred additional pharmaceutical; however, Windecker et al. teach that rapamycin (also known as sirolimus) has powerful anti-proliferative and anti-migratory drug properties on vascular smooth muscle cells (see page 1089 column 1 paragraph 1 lines 1-5). In addition, Windecker et al. go on to teach that its incorporation into biocompatible polymers, suitable for stent based drug delivery, has been successful (see page 1089 column 1 paragraph 1 lines 5-7). One of ordinary skill in the art at the time of the invention, would have found it obvious to couple the device of Tseng et al. with the teachings of Windecker et al. to produce a stent (an implantable medical device) containing drug depots capable of controllably releasing therapeutic dosages of trichostatin A and rapamycin, an anti-proliferative. Tseng et al. teach that the drug depots include one or more polymers (see claim 6), but do not specifically describe the polymer-drug configuration as a coating on the stent device. Chudzik et al. teach that the placement of devices within the body prompts a variety of complications including hyperplasia and restenosis (see paragraph 3 lines 3-9). In addition, Chudzik et al. go on to teach that to ameliorate these negatives, devices themselves can be made to provide bioactive compounds (see paragraph 4

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lines 1-2 and 6-7). Chudzik et al. disclose a particular medical device to solve this issue, which includes a polymer coating that contains a bioactive agent, such that the agent is controllably released (see claims 1, 11, and 30). One skilled in the art at the time of the invention would have found it obvious to use the coating configuration of Chudzik et al. for the drug depot containing stent of the Windecker et al. modified Tseng et al. device. Since both inventions address the issue of the body's response to medical device implantation, and specifically restenosis (see Tseng et al. paragraph 132 and Chudzik et al. paragraph 3 lines 1-6 and 10), one skilled in the art would have had a reasonable expectation of success for the combination, where the drug depot containing stent device of Tseng et al. includes trichostatin A and rapamycin (in light of Windecker et al.), capable of controllable release at therapeutic dosages, and contained within a polymeric coating (in light of Chudzik et al.). Thus, instant claims 1, 2, 4-7, and 9-11 are obvious over Tseng et al. in light of Windecker et al. and Chudzik et al.

Claims 3 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tseng et al. in light of Carter et al. (US Pregrant Publication No. US 2002/0013616 A1), Windecker et al. and Chudzik et al.

As previously described Tseng et al. modified by both Windecker et al. and Chudzik et al. teach a stent device with drug depots containing trichostatin A and rapamycin, where the drugs are contained within a polymeric coating and are able to be controllably released in therapeutic dosages (see preceding paragraph). The modified Tseng et al. reference also teaches that the reasoning for incorporating the trichostatin A, the HDAC inhibitor, within the stent device is for dealing with the issue of restenosis following stent implantation (see Tseng et al. paragraphs 29, 31, and 37). Tseng et al. modified by Windecker et al. and Chudzik et al. does not specifically teach stent grafts containing the drug depots with controllable release

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capabilities. Carter et al. teach that stents are commonly used to clear obstructions and to repair damage to vascular tissue (see paragraph 39 lines 2-5). Carter et al. go on to teach that stent grafts are a common name for a modification of stents where a flexible covering is attached to the stent frame (see paragraph 39 lines 10-12) and that the implantation process for stents, as a whole, carries with it the risk of causing restenosis (see paragraph 50 line 9). Since stent grafts are a modification of stents and also subject to post-implantation restenosis, it would have been obvious to one skilled in the art at the time of the invention to further modify the invention of Tseng et al. in light of Windecker et al. and Chudzik et al., by incorporating the controllably releasing drug depots, configured as a polymeric coating containing trichostatin A and rapamycin, within a stent-graft device. Therefore, instant claims 3 and 8 are obvious over Tseng et al. in light of Windecker et al., Chudzik et al., and Carter et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 6, 7, 8, 10 and 11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8, 9, 10, and 12 of copending Application No. 10/805,736 (US Pregrant Publication No. US 2005/0209688) in light of Pribluda et al. (Cancer and Metastasis). Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant application claims a medical device comprising an implantable structure, both a histone deacetylase (HDAC) inhibitor and an anti-proliferative, specifically rapamycin, in therapeutic dosages releasably affixed to the structure, for the treatment of restenosis (see instant claims 6 and 10). This recitation by the applicants broadly includes all implantable structures, such as a biocompatible implantable structure, as well as the rapamycin claimed in application '736. In addition claims 9, 10, and 12 further limit claim 8 of application '736 in exactly the same fashion as instant claims 7, 8, and 11 further limit instant claim 6. The instant claims teach all the limitations of claims 8, 9, 10, and 12, except the specific use of 2-methoxyestradiol, as claimed by application '736. The HDAC inhibitor has the property of inhibiting cellular proliferation (see Tseng et al. paragraph 121 lines 1-4). Pribluda et al. teach that 2-methoxyestradiol also has the property of inhibiting cellular proliferation (see page 173 column 2 paragraph 1 lines 1-8). One skilled in the art at the time of invention would have found it obvious to exchange one anti-proliferative drug for another in the instant application, namely use 2-methoxyestradiol instead of the HDAC inhibitor in the medical device. Therefore, instant claims 6, 7, 8, 10 and 11 are provisionally rejected as being unpatentable over application 10/805, 736 in light of Pribluda et al.

Claims 6-8, and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12-18 of copending Application No. 10/796,397 (US Pregrant Publication No. US 2005/0202059) in light of Waksman (Cardiovascular Radiation Medicine) and Hardman et al. (Goodman and Gilman's: The Pharmacological Basis of Therapeutics). Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant application claims a medical device comprising an implantable structure, both a HDAC inhibitor and an anti-proliferative, specifically rapamycin, present in therapeutic dosages, releasably affixed to the structure for the treatment of restenosis following vascular injury (see instant claims 6 and 10). Waksman teaches that the pathology of restenosis involves the hyper-proliferation of cells and matrix synthesis, elastic recoil (when balloon angioplasty has been employed), and late vascular contraction resulting in a decrease in vessel diameter (see page 226 column 2 paragraph 1 lines 5-11). Waksman goes on to teach that strategies for preventing restenosis have focused on anti-proliferative therapies and intervention into the cell cycle (see page 227 column 1 paragraph 1 lines 5-9). Topoisomerase I inhibitors interfere with the cell cycle by blocking the religation of DNA that is ordinarily facilitated by topoisomerase and ultimately results in cell death (see Hardman et al. page 1423 column 1 paragraph 2 lines 8-9 and paragraph 3 lines 1-10). This interference in the cell cycle focuses on the S-phase for eliciting its cytotoxic effect (see Hardman et al. page 1423 column 1 paragraph 3 lines 10-12). The invention of instant claims 6-8 and 10 contains all the limitations of the invention in claims 12-18 in application '397, except that the instant application uses trichostatin A, a HDAC inhibitor, instead of a topoisomerase I inhibitor. Since it has been established in the art that targeting both proliferation and the cell cycle are viable strategies for treating restenosis, one of ordinary skill in the art at the time of the invention would have found it obvious to replace the HDAC inhibitor in the instant invention with a topoisomerase I inhibitor, in

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effort to treat the causes of restenosis. Therefore, instant claims 6-8, and 10 are provisionally rejected as being unpatentable over claims 12-18 of application 10/796,397 in light of Hardman et al. and Waksman.

Claims 6-8 and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-16 of copending Application No. 10/805,722 (US Pregrant Publication No. US 2005/0208092) in light of Hardman et al. The same reasoning presented in the preceding paragraph holds true in the comparison of instant claims 6-8 and 10 with claims 11-16 of application '722. In this instance, instead of a HDAC inhibitor, as is used in the instant invention, application '722 uses a cytostatic glucoside. The specific cytostatic glucosides claimed in '722 are epipodophyllotoxins (teniposide and etoposide) or podophyllotoxins (podofilox), which both interfere with the cell cycle, but act via difference mechanisms; namely, each group of drugs cause cell death through DNA strand breakage or the arrest of cells in mitosis (see Hardman et al. page 1423 column 2 lines 1-10). It has been established in the art that targeting both proliferation and the cell cycle are viable strategies for treating restenosis, thus, one of ordinary skill in the art at the time of the invention would have found it obvious to replace the HDAC inhibitor in the instant invention with a cytostatic glucoside, in effort to treat the causes of restenosis. Therefore, instant claims 6-8 and 10 are provisionally rejected as being unpatentable over claims 11-16 of application 10/805,722 in light of Hardman et al.

Claims 6, 8, and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 11/149, 466 (US Pregrant Publication No. US 2005/0249776). Instant claims 6

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and 10 are drawn to an implantable structure with rapamycin and an HDAC inhibitor in releasably affixed, therapeutic dosages. As these claims broadly include the limitations of claim 1 and 2 of application '466, they are not patentably distinct from the claims of the instant application. In addition instant claim 8 and claim 2 of '466 provide the same additional limitation to the claims from which they depend and are also patently indistinct from one another. Therefore, instant claims 6, 8, and 10 are provisionally rejected as being unpatentable over claims 1-3 of application 11/149, 466.

Claims 6-8 and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4-6 of copending Application No.11/131, 720 (US Pregrant Publication No. US 2005/0249775). Instant claims 6 and 10 are drawn to an implantable structure with rapamycin and an HDAC inhibitor in releasably affixed, therapeutic dosages. As these claims broadly include the limitations of claim 1 and 4 of application '720, they are not patentably distinct from the claims of the instant application. In addition, instant claims 8 and 10 further limit the claims from which they depend in the same way as claims 5 and 6 of '720 and are also patently indistinct from one another. Therefore, instant claims 6-8 and 10 are provisionally rejected as being unpatentable over claims 1 and 4-6 of application 11/131, 720

The preceding are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Caralynne Helm whose telephone number is 571-270-3506. The examiner can normally be reached on Monday through Thursday 8-4 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Caralynne Helm
Examiner
Art Unit 1609

CH

 8/27/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER